



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Bastian Nuyen et al.                      Art Unit : Unknown  
Serial No. : 09/622,433                                      Examiner : Unknown  
Filed : May 10, 2002  
Title : PHARMACEUTICAL FORMULATION OF A DIDEMNIN COMPOUND

**MAIL STOP AMENDMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Copies of the references listed on the attached form PTO-1449 are enclosed.

Reference AN is a non-English language document. Pursuant to MPEP § 609, an English language abstract is included with each of the reference AN to fulfill the requirement for providing a concise explanation of relevance for non-English language documents.

Applicants wish to bring to the Examiner's attention the following co-pending non-Provisional applications:

<u>Serial No.</u>	<u>Applicants</u>	<u>Filed</u>	<u>Status</u>
10/312,341	Rodriguez et al.	December 24, 2002	Pending
10/130,097	Faircloth et al.	August 29, 2002	Pending
10/357,759	Rinehart et al.	February 4, 2002	Pending
10/398,835	Lazaro et al.	April 9, 2003	Pending
10/492,659	Mangues et al.	April 13, 2004	Pending

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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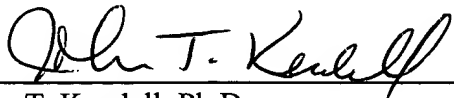
Applicant : Bastian Nuyen et al.  
Serial No. : 09/622,433  
Filed : May 10, 2002  
Page : 2 of 2

Attorney's Docket No.: 14620-012US1 / JC/USP78531

This statement is being filed within three months of the filing date of the application or before the receipt of a first Office Action on the merits. Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No.: 14620-012US1.

Respectfully submitted,

Date: October 18, 2004

  
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Sheet 1 of 3

Substitute Form PTO-1449 (Modification)	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 14620-012US1	Application No. 09/622,433
<b>Information Disclosure Statement by Applicant</b> (Use several sheets if necessary) (37 CFR §1.98(b))		Applicant Bastian Nuyen et al.	
		Filing Date May 10, 2002	Group Art Unit

### U.S. Patent Documents

Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AA	4,493,796	01/15/1985	Rinehart, Jr.			
	AB	4,670,262	06/02/1987	Battelli et al.			
	AC	5,294,603	03/15/1994	Rinehart			
	AD	5,462,726	10/31/1995	Lodge			
	AE	5,834,586	11/10/1998	Rinehart et al.			
	AF	6,034,058	03/07/2000	Rinehart et al.			
	AG	6,153,731	11/28/2000	Rinehart et al.			
	AH	6,156,724	12/05/2000	Rinehart et al.			
	AI	6,710,029	03/23/2004	Rinehart et al.			

### Foreign Patent Documents or Published Foreign Patent Applications

Examiner Initial	Desig. ID	Document Number	Publication Date	Country or Patent Office	Class	Subclass	Translation	
							Yes	No
	AJ	0 048 149 A1 ✓	03/24/1982	EPO				
	AK	0 393 883 ✓	10/24/1990	EPO				
	AL	WO 91/04985 ✓	04/18/1991	WIPO				
	AM	WO 93/00362 ✓	01/07/1993	WIPO				
	AN	2 102 322 ✓	07/16/1997	Spain			Abstract Only	
	AO	WO 98/17275 ✓	04/30/1998	WIPO				
	AP	WO 98/17302 ✓	04/30/1998	WIPO				
	AQ	WO 99/42125 ✓	08/26/1999	WIPO				
	AR	WO 01/35974 ✓	05/25/2001	WIPO				
	AS	WO 01/76616 ✓	10/18/2001	WIPO				
	AT	WO 02/02596 ✓	01/10/2002	WIPO				
	AU	WO 02/030441 ✓	04/18/2002	WIPO				
	AV	WO 03/033013 ✓	04/24/2003	WIPO				

### Other Documents (include Author, Title, Date, and Place of Publication)

Examiner Initial	Desig. ID	Document
	AW	Ady-Vago, N. et al., "L-Carnitine as a Protector Against Aplidine Induced Skeletal Muscle Toxicity", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 42, pp. 545 (March, 2001)

Examiner Signature

Date Considered

EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute Form PTO-1449 (Modified)  <b>Information Disclosure Statement by Applicant</b> (Use several sheets if necessary)  (37 CFR §1.98(b))	U.S. Department of Commerce Patent and Trademark Office	Attorney's Docket No. 14620-012US1	Application No. 09/622,433
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U.S. Patent Documents							
Examiner Initial	Desig. ID	Document Number	Publication Date	Patentee	Class	Subclass	Filing Date If Appropriate
	AX	Bergeron, Raymond J. et al., "Antineoplastic and Antiherpetic Activity of Spermidine Catecholamide Iron Chelators", <u>Biochemical and Biophysical Research Communications</u> , Vol. 121, No. 3, pp. 848-854 (1984)					
	AY	Broggini, M. et al., "Aplidine Blocks VEGF Secretion and VEGF/VEGF-RI Autocrine Loop in a Human Leukemic Cell Line", <u>11<sup>th</sup> NCI-EORTC-AACR on New Drugs in Cancer Therapy</u> , Amsterdam (2000), Abstract 214.					
	AZ	Chapa, A.M. et al., "Influence of Intravenous L-Carnitine Administration in Sheep Preceding an Oral Urea Drench <sup>1,2</sup> ", <u>Journal of Animal Science</u> , Vol. 76, No. 11, pp. 2930-2937 (1998)					
	AAA	Depenbrock, H. et al., "In vitro activity of aplidine, a new marine-derived anti-cancer compound, on freshly explanted clonogenic human tumour cells and haematopoietic precursor cells", <u>British Journal of Cancer</u> , Vol. 78, No. 6, pp. 739-744 (1998)					
	ABB	Erba, E. et al., "Cell cycle phases perturbations induced by new natural marine compounds", <u>Annals of Oncology</u> , Vol. 7, Supplement 1, #283, pp. 82 (1996)					
	ACC	Faircloth, G. et al., "Aplidine (APL) is a novel marine-derived depsipeptide with in vivo antitumor activity", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 39, #1551, pp. 227 (1998)					
	ADD	Faircloth, G. et al., "Dehydrididemnin B (DDB) a new marine derived anti-cancer agent (MDA) with activity against experimental tumor models" and "Biological activity of thiocoraline. A new depsipeptide from a marine micromonospora", <u>Annals of Oncology</u> , Vol. 7, Supplement 1, #111 and #112, pp. 34 (1996)					
	AEE	Faircloth, G. et al., "Preclinical characterization of Aplidine (APD), a new marine anticancer depsipeptide (MADEP)", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 38, #692, pp. 103 (1997)					
	AFF	Faircloth, G. et al., "Preclinical development of aplidine, a novel marine-derived agent with potent antitumor activity", <u>Annals of Oncology</u> , Vol. 9, Supplement 2, #129, pp. 34 (1998)					
	AGG	Faircloth, G. et al., "Schedule-dependency of aplidine, a marine depsipeptide with antitumor activity", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 40, #2612, pp. 394-395 (1999)					
	AHH	Geldof, Albert A. et al., "Cytotoxicity and neurocytotoxicity of new marine anticancer agents evaluated using in vitro assays", <u>Cancer Chemother. Pharmacol.</u> , Vol. 44, pp. 312-318 (1999)					
	AII	Genin, Michael J. et al., "Synthesis and Crystal Structure of a Peptidomimetic Containing the (R)-4, 4-Spiro Lactam Type-II $\beta$ -Turn Mimic", <u>Journal of Organic Chemistry</u> , Vol. 58, No. 8, pp. 2334-2337 (1993)					
	AJJ	Gomez-Fabre, P.M. et al., "Polamine contents of human breast cancer cells treated with the cytotoxic agents chlorpheniramine and dehydrididemnin B", <u>Cancer Letters</u> , Vol. 113, Nos. 1, 2, pp. 141-144 (1997)					
	AKK	Jimeno et al., "A Correlation of Selective Antitumor Activities of the Marine-Derived Compound Aplidine Using Different Models", <u>10<sup>th</sup> NCI-EORTC-AACR Symposium on Molecular Targets and Cancer Therapeutics</u> , Washington (1999), Abstract 311.					
	ALL	Jou, Gemma et al., "Total Synthesis of Dehydrididemnin B. Use of Uronium and Phosphonium Salt Coupling Reagents in Peptide Synthesis in Solution", <u>Journal of Organic Chemistry</u> , Vol. 62, No. 2, pp. 354-366 (1997)					
	AMM	Lobo, C. et al., "Effect of Dehydrididemnin B on Human Colon Carcinoma Cell Lines", <u>Anticancer Research</u> , Vol. 17, No. 1A, pp. 333-336 (1997)					

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(37 CFR §1.98(b))			

### U.S. Patent Documents

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	ANN	Luber-Narod, J. et al., "In Vitro Safety Profile of Aplidine, A Marine Natural Product with Chemotherapeutic Potential", <u>Proceedings of the AACR</u> , Vol. 42, Abstract 374, March 2001.					
	AOO	Mastbergen, S.C. et al., "Cytotoxicity and neurocytotoxicity of aplidine, a new marine anticancer agent evaluated using in vitro assays", <u>Annals of Oncology</u> , Vol. 9, Supplement 2, #131 (1998)					
	APP	Montgomery, D.W. et al., "Didemnin B Alters the Specific Binding of Prolactin to Human Lymphocytes and Decreases the Circulating Level of Prolactin in Mice", <u>Federal Proceedings</u> , Vol. 44, No. 3, pp. 634, #1311 (1985)					
	AQQ	Montgomery, David W. et al., "Didemnin B: A New Immunosuppressive Cyclic Peptide with Potent Activity In Vitro and In Vivo", <u>Transplantation</u> , Vol. 40, No. 1, pp. 49-56 (1985)					
	ARR	Nuijen, B. et al., "Pharmaceutical development of anticancer agents derived from marine sources", <u>Anti-Cancer Drugs</u> , Vol. 11, pp. 793-811 (2000)					
	ASS	Raymond, Eric et al., "Preliminary Results of a Phase I and Pharmacokinetic Study of Aplidine Given as a 24-hour Infusion Every 2 Weeks in Patients With Solid Tumors and Non Hodgkin's Lymphomas", <u>Proceedings of the American Association for Cancer Research</u> , Vol. 41, #3886 (2000)					
	ATT	Rinehart, K., "Didemnin and its Biological Properties", <u>Escom</u> , pp. 626-631 (1987).					
	AUU	Rinehart, Kenneth L. et al., "Biologically Active Peptides and Their Mass Spectra", <u>Pure and Applied Chemistry</u> , Vol. 54, No. 12, pp. 2409-2424 (1982)					
	AVV	Rinehart, Kenneth L. et al., "Didemnins and Tunichlorin: Novel Natural Products from the Marine Tunicate <i>Trididemnum Solidum</i> ", <u>Journal of Natural Products</u> , Vol. 51, No. 1, pp. 1-21 (1988)					
	AWW	Rinehart, Kenneth L. et al., "Total Synthesis of Didemnins A, B and C <sup>1,2</sup> ", <u>Journal of the American Chemical Society</u> , Vol. 109, No. 22, pp. 6846-6848 (1987)					
	AXX	Rinehart, Kenneth L., Jr. et al., "Antiviral and antitumor compounds from tunicates <sup>1,2</sup> ", <u>Federation Proceedings</u> , Vol. 42, No. 1, pp. 87-90 (1983)					
	AYY	Rinehart, Kenneth L., Jr. et al., "Didemnins: Antiviral and Antitumor Depsipeptides from a Caribbean Tunicate", <u>Science</u> , Vol. 212, No. 4497, pp. 933-935 (1981)					
	AZZ	Rinehart, Kenneth L., Jr. et al., "Structure of the Didemnins, Antiviral and Cytotoxic Depsipeptides from a Caribbean Tunicate <sup>1</sup> ", <u>Journal of the American Chemistry Society</u> , Vol. 103, No. 7, pp. 1857-1859 (1981)					
	AAAA	Sakai, Ryuichi et al., "Structure - Activity Relationships of the Didemnins <sup>1,2</sup> ", <u>Journal of Medicinal Chemistry</u> , Vol. 39, No. 14, pp. 2819-2834 (1996)					
	ABBB	Seebach, Dieter et al., "Alkylation of Amino Acids without Loss of the Optical Activity: Preparation of $\alpha$ -Substituted Proline Derivatives. A Case of Self-Reproduction of Chirality <sup>1,2</sup> ", <u>Journal of the American Chemical Society</u> , Vol. 105, No. 16, pp. 5390-5398 (1983)					
	ACCC	Urdiales, Jose L. et al., "Antiproliferative effect of dehydrodidemnin B (DDB), a depsipeptide isolated from Mediterranean tunicates", <u>Cancer Letters</u> , Vol. 102, Nos. 1,2, pp. 31-37 (1996)					
	ADDD	Vervoort, Helene et al., "Tamandarins A and B: New Cytotoxic Depsipeptides from a Brazilian Ascidian of the Family Didemnidae", <u>The Journal of Organic Chemistry</u> , Vol. 65, No. 3, pp. 782-792 (2000)					

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